PCN35
SURVIVAL AFTER LOCOREGIONAL RECURRENCE OR SECOND PRIMARY BREAST CANCER: IMPACT OF THE DISEASE-FREE INTERVAL
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OBJECTIVES: The association between the disease-free interval (DFI) and survival after a locoregional recurrence (LRR) or second primary (SP) breast cancer remains uncertain. The objective of this study is to clarify this association to obtain more information on expected prognosis. **METHODS:** Women first diagnosed with early breast cancer between 2003-2006 were selected from the Netherlands Cancer Registry. LRRs and SP tumours within five years of first diagnosis were examined. The five-year period was subsequently divided into three equal intervals. Prognostic significance of the DFI on survival after a LRR or SP tumour was determined using Kaplan-Meier estimates and multivariable Cox regression analysis. Follow-up was complete until January 1,2013. **RESULTS:** A total of 36,255 women was included in the analysis. LRRs or SP tumours were diagnosed in 1,646 (4.5%) patients: 55% developed a LRR and 45% SP breast cancer. Longer DFI was strongly and independently related to an improved survival after a LRR (long versus short: HR 0.63, 95% CI 0.46-0.86; medium versus short HR 0.80, 95% CI 0.64-1.00; P for trend 0.01). Other factors related to improved survival after LRR were younger age (<70 years) and surgical removal of the recurrence. No significant association was found between DFI and survival after SP tumours. **CONCLUSIONS:** This is the first study to explore the association between the DFI and survival after recurrence in a nationwide population-based cancer registry. The DFI before a LRR is an independent prognostic factor for survival, with a longer DFI predicting better prognosis.

PCN36
LONG TERM SURVIVAL OF PATIENTS WITH VARIOUS LUNG CANCER HISTOLOGY IN SEER BETWEEN 2004-2011
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OBJECTIVES: Overall survival (OS) data from clinical trials in oncology are often incomplete, thus modelling over the lifetime horizon requires long term extrapolation and it is a critical input to cost-effectiveness studies. Data from the Surveillance, Epidemiology, and End Results (SEER) program may provide good validation on the long term OS. The objective was to examine the parametric functions that best fit data in lung cancer (LC) of various histologies in SEER. **METHODS:** SEER data (2004-2011) were analyzed for patients diagnosed with stage IV small cell, large cell, squamous cell carcinoma and adenocarcinoma of the lung with complete follow-up. Mean age was 68.03 (sd 11.67) and 55.5% were males, with varying baseline age and gender distribution by histology. Treatment status could not be established. Parametric models for OS were fitted using exponential, Gompertz, loglogistic, lognormal, and Weibull distributions. Models were fitted with and without covariates. Fits were inspected and compared graphically using survival and quantile-quantile plots, and statistically using the Akaike Information Criterion (AIC). Modelled mean life expectancy results were compared to the restricted mean life expectancy of the Kaplan-Meier estimator. **RESULTS:** The lognormal distribution was found to have the best fit within the SEER population, both with and without covariates indicating that a small proportion of patients survive for a long time despite the poor general prognosis of any type of LC. Loglogistic and gamma distributions were 2nd and 3rd best, followed by Weibull, Gompertz and exponential, for all histologies. The last three fitted the data poorly, and underestimated mean life expectancy. **CONCLUSIONS:** Only small proportions of LC patients are alive at 5-8 years, nevertheless the mean OS estimates are impacted by the choice of survival function. The lognormal distribution fit best across all histologies indicating a higher propotion of patients alive than estimated with Weibull models.

PCN37
IMPACT OF HOSPITAL VOLUME ON BREAST CANCER OUTCOME: A POPULATION BASED STUDY IN THE NETHERLANDS
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OBJECTIVES: For low-volume tumours, high surgical hospital volume is associated with better survival. For high volume tumours like breast cancer this association is unclear. The aim of this study is to determine to what extent the yearly surgical hospital breast cancer volume is associated with overall survival. **METHODS:** All patients, diagnosed with primary invasive non-metastatic breast cancer in the period 2001-2005, were selected from the Netherlands Cancer Registry. Hospitals were grouped by their annual volume of surgery for invasive breast cancer. Cox proportional hazard models were used including patient and tumour characteristics as covariates. Follow-up was completed until the 1thof February 2013. Primary endpoint was 10-year overall survival rate. **RESULTS:** In total 58,982 patients with invasive non-metastatic breast cancer were diagnosed during the period 2001-2005. Hospitals were grouped by their (mean) annually surgical volume: <75 (n=19), 75-99 (n=30), 100-149 (n=29), 150-199 (n=9) and ≥200 (n=14). The 10-year observed survival rates were 77%, 81%, 80%, 82% and 82%, respectively. After case-mix adjustment patients in low volume hospitals had a HR of 1.08 (<75 vs ≥200; 95%CI 1.02-1.14). Age at diagnosis (continuous, HR 1.05, 95%CI 1.05-1.05), socioeconomic status (lowest vs highest; HR 1.12, 95%CI 1.07-1.16), grade (high vs low, HR 1.72, 95%CI 1.63-1.82), tumour size (2-5 cm vs 1-2 cm; HR 1.46, 95%CI 1.40-1.51), and a higher number of positive lymph nodes (1-3 vs 0; HR 1.40, 95%CI 1.34-1.46 and >10 vs 0; HR 3.19, 95%CI 3.00-3.39) influenced death, all to a larger extent than surgical volume did. **CONCLUSIONS:** In the Netherlands, surgical hospital volume influences 10-year overall survival only marginally, and far less than patient and tumour characteristics. No difference in survival was revealed for invasive non-metastatic breast cancer patients in hospitals with 75-99 operations per year compared with hospitals with over 200 operations per year.

PCN38
SIMULATION MODEL OF IBRUTINIB IN TREATMENT OF RELAPSED OR REFRACTORY MANTLE CELL LYMPHOMA (MCL)
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OBJECTIVES: For patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL), prognosis is poor, with a median survival of one to two years, and treatment options are very limited. In a recent phase II trial (PCYCY-1104), Ibrutinib (Imbruvica™), a first-in-class oral once a day covalent Bruton's tyrosine kinase inhibitor, was associated with a median progression-free survival (PFS) of 13.9 months. After a median follow-up of 15.3 months, 63% of patients were alive. The aim of the current study was to evaluate the projected life years (LYs) and quality-adjusted LYs (QALYs) associated with ibrutinib and other treatments for R/R MCL. **METHODS:** Patients with R/R MCL were simulated to receive treatment in a health state, survival partition model. Patients received ibrutinib, bendamustine and rituximab (BR), fludarabine, mitoxantrone, and cyclophosphamide (FMC), temsirolimus, or other comparators until death or until progression of disease, at which point they were modeled to receive a subsequent line of treatment or best supportive care. Clinical inputs for ibrutinib were informed by PCYC-1104 trial data; OS was extrapolated to estimate survival outcomes. Clinical inputs for comparators were informed by published sources identified through a systematic literature review. Utility values were informed by published studies. Outcomes were discounted by 3.5%. **RESULTS:** Treatment with ibrutinib resulted in better health outcomes, incrementally increasing overall LYs by 0.92, 0.86, and 0.92 and PFS LYs by 0.87, 0.87, and 0.87 compared to BR, FMC, and temsirolimus, respectively. Ibrutinib was associated with 0.71, 0.70, and 0.72 overall incremental QALYs compared to BR, FMC, and temsirolimus, respectively. **CONCLUSIONS:** Compared with other therapies, Ibrutinib yielded an average incremental benefit of 0.90 LYs for R/R MCL patients, largely driven by the significant incremental improvement in duration of PFS. Currently a phase III trial is ongoing, the data from which will be used to validate the model.

PCN39
THE BENEFIT OF HER-2 TARGETED THERAPIES ON OVERALL SURVIVAL OF PATIENTS WITH METASTATIC BREAST CANCER – A SYSTEMATIC REVIEW
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OBJECTIVES: This study was aimed at evaluating the overall survival (OS) gains associated with HER-2 directed therapies in patients with metastatic breast cancer. **METHODS:** A bibliographic search was conducted in the MEDLINE (PubMed) and in the Cochrane Central Register of Controlled Trials databases, from their inception through March, 2014. Only phase III clinical trials (RCTs) including HER2-positive metastatic breast cancer patients have been included in this review, irrespective of the treatment administered (i.e., chemotherapy and/or hormone therapy, chemotherapy and/or hormone therapy plus HER2-targeted therapy). OS was defined as time from randomisation until the occurrence of death from any cause. Studies have been grouped according to the line of treatment, i.e. first-line or second-line or beyond. **RESULTS:** Seventeen RCTs were eligible for inclusion, of which 12 assessed therapies targeting metastatic breast cancer HER2+ in the first line setting. OS improved from 20.3 months in the first RCT (standard chemotherapy; Slamon et al, 2001) evaluating HER-2 targeting therapies to 48 months (estimated median OS) in the study of Swain and colleagues (2013), with triple combination of pertuzumab, trastuzumab and docetaxel. Four studies evaluated OS of HER-2 targeting therapies in second-line setting of metastatic breast cancer. The OS in second-line setting improved from 15.3 months (capecitabine; Cameron et al, 2008) to 30.7 months (trastuzumab emtancine; Verma et al, 2012). In the third-line setting, the association of lapatinib + trastuzumab has demonstrated to improve OS in 4.5 months compared with lapatinib alone (14 months vs 9.5 months; Blackwell et al, 2012). **CONCLUSIONS:** The HER-2 directed therapies had an undeniable benefic impact in the overall survival of patients with HER-2 positive metastatic breast cancer. Triple combination of docetaxel, pertuzumab and trastuzumab is associated with a survival extent of more than 3.5 years, compared with a life expectancy of 1,5 years achieved 13 years ago.

PCN40
SIMULATION MODEL OF IBRUTINIB FOR CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) WITH PRIOR TREATMENT
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OBJECTIVES: Treatment options for chronic lymphocytic leukemia (CLL) who received prior therapy are limited; no standard of care exists. In a recent phase III clinical trial (PCYC-1112), ibrutinib, an oral, once-a-day, first-in-class covalent Bruton's tyrosine kinase inhibitor, was associated with improved progression-free survival (PFS, HR=0.215) and overall survival (OS, HR=0.387) compared with ofa-